HPV Prevention: Where Are We and Where Do We Need to Go

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Disclosures

• I have no financial relationships to disclose

• I do not intend to discuss off-label uses for FDA-approved products
What you need to know about HPV
HPV is the most common sexually transmitted infection in the U.S.

- Over 6.2 million new infections every year
- Nearly three-fourths new infections in 15-24yo

Dunne et al. JAMA. 2007;297:813-819
Prevalence of HPV Among FEMALES 14 to 59 years

Dunne et al. JAMA. 2007;297:813-819
Prevalence of HPV Among MALES 18 to 70 years

Age Distribution of Oncogenic HPV Infections (p trend=0.354)

% 45 40 35 30 25 20 15 10 5 0

18-19 yrs 20-24 yrs 25-29 yrs 30-34 yrs 35-39 yrs 40-44 yrs 45-70 yrs

Giuliano A R et al. Cancer Epidemiol Biomarkers Prev 2008;17:2036-2043
Prevalence of HPV Among Females 14 to 59 years

By 50 years old, 80% of women will have acquired a genital HPV infection…

HPV is ubiquitous

By 50 years old, 80% of women will have acquired a genital HPV infection…

Most will not develop cancer

CDC Pink Book: www.cdc.gov/vaccines/pubs/pinkbook/hpv.html
Skin to skin contact!

HPV can spread through anogenital region

- Condoms only partially effective prevention
- Some adolescents found to test positive for vaginal HPV prior to first vaginal sexual intercourse

HPV-Related Disease in Adults

• Genital Warts
• Anogenital dysplasias and carcinomas
• Head and neck cancers
# HPV-Related Cancer in 2014

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>New Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral, Pharyngeal</td>
<td>42,440</td>
<td>8390</td>
</tr>
<tr>
<td>Cervical</td>
<td>12,360</td>
<td>4020</td>
</tr>
<tr>
<td>Vaginal and Vulvar</td>
<td>8020</td>
<td>1910</td>
</tr>
<tr>
<td>Anal</td>
<td>7210</td>
<td>950</td>
</tr>
<tr>
<td>Penile</td>
<td>1649</td>
<td>320</td>
</tr>
</tbody>
</table>

### HPV-Related Cancers in 2014

#### Incidence of HPV-related oral pharyngeal and anal carcinomas are increasing

- Particularly among **males**
- **60+%** of oropharyngeal carcinomas positive for HPV 16

<table>
<thead>
<tr>
<th></th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Both Sexes</td>
<td>Male</td>
</tr>
<tr>
<td>All Sites</td>
<td>1,665,540</td>
<td>855,220</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>42,440</td>
<td><strong>30,220</strong></td>
</tr>
<tr>
<td>Tongue</td>
<td>13,590</td>
<td>9,720</td>
</tr>
<tr>
<td>Mouth</td>
<td>11,920</td>
<td>7,150</td>
</tr>
<tr>
<td>Pharynx</td>
<td>14,410</td>
<td>11,550</td>
</tr>
<tr>
<td>Other oral cavity</td>
<td>2,520</td>
<td>1,800</td>
</tr>
<tr>
<td>Anus, anal canal, &amp; anorectum</td>
<td>7,210</td>
<td>2,660</td>
</tr>
</tbody>
</table>

HPV Oropharyngeal Cancers in U.S.

- Increase in oropharyngeal cancers in past decades despite decrease in tobacco use
  - Tobacco and alcohol remain risk factors
  - Many HPV+ cancers among never smokers

- If trend continues oropharyngeal HPV-related cancers will exceed incidence of cervical cancer in coming years
  - More MEN with HPV-related cancer than women

HPV Oropharyngeal Cancers in U.S.

- Transmission is oral sex
  - Though not completely understood

- Why increase in younger individuals?
  - Different sexual norms
  - Oral sex at an earlier age
  - Decrease in other tobacco-related cancers

- Greater prevalence in men?
  - HPV burden in cervix greater than penis

- Oral HPV detected in 3-5% of adolescents, and 5-10% adults

Vaccination against HPV does NOT affect sexual behavior
HPV Prevention: Vaccination

HPV4 – Gardasil (Merck)
HPV2 – Cervarix (GSK)
HPV Vaccine: HPV4

• First FDA licensed indications: June 8, 2006
• For females aged 9-26 years, quadrivalent HPV vaccine is indicated for prevention of the following diseases caused by HPV types 6, 11, 16, and 18:
  – Genital warts
  – Cervical cancer
  – Cervical adenocarcinoma in situ
  – Cervical intraepithelial neoplasia grade 2 and grade 3
  – Cervical intraepithelial neoplasia grade 1
  – Vulvar intraepithelial neoplasia grade 2 and grade 3
  – Vaginal intraepithelial neoplasia grade 2 and grade 3

FDA=US Food and Drug Administration.
www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM094042
Since that time, 2 additional indications have been licensed for quadravalent vaccine:

- Vaccination of **boys and men** aged 9 through 26 years for the prevention of genital warts caused by HPV types 6 and 11

- Vaccination of **males and females** aged 9 through 26 years for the prevention of anal cancer and associated precancerous lesions due to HPV types 6, 11, 16, and 18

www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM094042
A bivalent vaccine was licensed October 26, 2009

For females aged 10-25 years, the bivalent HPV vaccine is indicated for prevention of the following diseases caused by **HPV types 16 and 18**:

- Cervical cancer
- Cervical adenocarcinoma in situ
- Cervical intraepithelial neoplasia grade 2 and grade 3
- Cervical intraepithelial neoplasia grade 1
• HPV immunization is recommended for all males and females
  – Target age: 11–12 years
  – Immunization may be initiated as young as age 9 years
Catch-up HPV immunization is recommended for:

- Females aged 13–26 years
- Males aged 13–21 years
- High-risk males aged 22–26 years
“Recommend” is the same language used by ACIP for all other childhood vaccines.
HPV vaccine should be offered to all adolescents and young adults regardless of:

- Sexual history
- History of abnormal Pap
- History of HPV positive Pap
- Sexual orientation
Vaccination Coverage in the U.S.
Achieving high coverage in Rwanda's national human papillomavirus vaccination programme

Brotherton, Lancet 2011; Cuzick BJC 2010; Ogilvie et al., 2010; Marc et al., 2010, NIS-Teen 2011.
Seven Years of Vaccinating Against HPV
HPV Vaccines are Safe

- > 60 million doses distributed in US
- Most common adverse events were mild
  - Sore arm, myalgias
- Serious adverse events: No patterns to suggest any events caused by the vaccine
- Findings similar to the safety of all other adolescent vaccines
“The events reported were consistent with events expected in healthy adolescent and adult populations.”

Human Papillomavirus Bivalent (Types 6, 11, 16, 18) Vaccine, Recombinant (Gardasil) Prescribing Information

“Causes of death among subjects were consistent with those reported in adolescent and adult female populations.”

Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant (Cervarix) Prescribing Information
Population-based, Post-licensure Observational Safety Studies of HPV4 Vaccine in US Females Aged 9–26 Years

<table>
<thead>
<tr>
<th>Organization</th>
<th>System or review</th>
<th>No. of doses evaluated</th>
<th>Description</th>
<th>Methods</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC</td>
<td>Vaccine Safety Datalink</td>
<td>600,559</td>
<td>Safety assessment of 7 prespecified health outcomes among female HPV4 vaccine recipients at 7 managed care organizations</td>
<td>Cohort design with weekly sequential analyses of electronic medical data</td>
<td>No statistically significant increase in risk for the outcomes monitored</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Postmarketing commitment to FDA</td>
<td>346,972</td>
<td>General study assessment of HPV4 vaccine after routine administration at 2 large managed care organizations</td>
<td>Self-controlled risk interval design, supplemented with medical record review</td>
<td>HPV4 vaccine associated with syncope on the day of vaccination and skin infections in the 2 weeks after vaccination</td>
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<td>Assessment of 16 prespecified autoimmune conditions after routine use of HPV4 vaccine at 2 large managed care organizations</td>
<td>Retrospective cohort using electronic medical data, supplemented with medical record review</td>
<td>No confirmed safety signals for the outcomes monitored</td>
</tr>
</tbody>
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Clinical Outcomes
Genital Warts, Females by Age Group, US, 2003-2010

Vaccine first introduced in United States (dashed line)

F MarketScan® Database
Flagg EW et al. AJPH 2013;108 (8):1428-35
Australia
Australia

- >80% of school-age girls are fully vaccinated
- High-grade cervical lesions have declined in women <18 years
- Among vaccine-eligible females, 93% decline in cases of genital warts
  - 82% decline among unvaccinated males of the same age

Genital Warts among Females < 26 years, Australia, 2004-2010

Vaccine first introduced in Australia in 2006 (dashed line)

73% decrease in genital warts

Challenges and Barriers to Vaccinating Adolescents
Challenges to Vaccinating Adolescents

- Knowledge
- School Requirements
- Access
- Concern about HPV
Less than 50% of 11-18-year-olds on Medicaid had a health maintenance visit in a 2-year period

Dempsey AF, Freed GL. Pediatrics 2010; 125;43.
Proportion of Medicaid-Enrolled Adolescents Receiving Problem Focused Care

Dempsey AF, Freed GL. Pediatrics 2010; 125;43.
Strategies to Vaccinate

• Capture missed opportunities
  – Non-primary care visits: acute care visits, urgent care, ED
  – Standing immunization orders
  – Extended immunization hours
    • Flu clinic model
  – HPV: normalize vaccination

• Recall system for subsequent doses
How we present the vaccine

Considerations & Solutions
“Sex during adolescence is for other peoples kids”

#1: Parents do not want to think about their kids being sexually active

#2: Immunization 101: Vaccines can only prevent disease you have not yet had
   - Important to immunize before exposure
   - Most parents do not know how immunizations work
For many parents this vaccine is simply ‘new’ and they have questions

• What does it do?
• Who is it for?
• Is it safe?
Potential Solutions
"HPV stands for human papillomavirus and causes genital warts and cervical cancer. It is a sexually-transmitted disease. Many kids become sexually active by age 14.

Do you want this vaccine for your 11 year-old?"
“Today your son is due for three routine vaccines which include meningitis vaccine; Tdap which is tetanus, diphtheria, and whooping cough; and HPV which is human papillomavirus vaccine. Someone will be right in to administer those vaccines and I look forward to seeing you next year.”
If questions arise about the HPV vaccine:

“Has anyone that you care about had cancer?”

“What was it like for them?  For you?”

“We can reduce the chances of your son having a cancer experience. Do you want to reduce the chances of your son having cancer?”

Approach to Consider: *Less is More*
Most Important Final Message

Your Recommendation Matters Most!